

62. A method for identifying an agent for treating an animal having a disorder characterized by loss-of-function of a patched gene comprising contacting one or more test agents with a cell having a patched loss-of-function phenotype and identifying those test agents that reverse at least in part the patched loss-of-function phenotype wherein test agents that reverse a portion of the patched loss of function phenotype are useful for treating an animal having a disorder characterized by loss-of-function of a patched gene.

63. A method for identifying an agent for treating a proliferative disorder characterized by loss-of-function of a patched gene, comprising:

- B'
- a. comparing the amount of expression of a reporter gene in a first recombinant mammalian cell in the presence of a test compound with the amount of expression in the absence of the compound, or with the amount of expression in a second recombinant cell; and
  - b. identifying test compounds that decrease the amount of expression of the reporter gene in the first recombinant cell in the presence of the compound compared to the amount of expression in the absence of the compound, or compared to the amount of transcription or product in the second recombinant cell, wherein:

the first recombinant cell contains a reporter gene construct and expresses patched;

the second recombinant cell is identical to the first recombinant cell, except that it does not express a functional wild-type patched; and

the reporter gene constructs contains:

- (i) a transcriptional control element that is stimulated by a patched-dependent intracellular signal that is generated by the interaction of a hedgehog protein with patched; and
- (ii) a reporter gene that encodes a detectable product and that is in operative association with the transcriptional control element;

wherein a test compound identified in step (b) is useful for treating a proliferative disorder characterized by loss-of-function of a patched gene.

64. The method of claim 63, wherein the amount of transcription is determined by measuring the amount of mRNA that is transcribed from said reporter gene.

sub F3 65. The method of claim 63, wherein the amount of transcription is measured by measuring the amount of reporter gene protein that is produced.

66. The method of claim 63, further comprising, prior to comparing the difference in the amount of transcription of the reporter gene, contacting the recombinant cell with a hedgehog agonist in an amount sufficient to change the level of transcription of said reporter gene.

67. The method of claim 63, wherein the reporter gene is selected from the group consisting of a gene encoding chloramphenicol acetyltransferase, a gene encoding firefly luciferase, a gene encoding bacterial luciferase, and a gene encoding alkaline phosphatase.

SUB D2  
68. The method of claim 63, wherein the transcriptional control region includes at least one regulatory element selected from the group consisting of transcriptional regulatory elements of a patched gene, a transcriptional regulatory elements of a gli gene, and a transcriptional regulatory elements of a PTHrP gene.

B1  
69. The method of claim 63, wherein the patched protein is encoded by a nucleic acid which hybridizes at 5 x SSC at 65° C to SEQ ID No. 18.

SUB E2  
70. The method of claim 63, wherein expression of the reporter gene occurs upon hedgehog stimulation, and compounds are selected by ability to inhibit the patched-dependent expression of the reporter gene.

71. The method of claim 63, wherein the cell having a patched loss-of-function phenotype is a basal cell carcinoma.

SUB C2  
72. A method for preparing an agent for inhibiting growth of cells characterized by loss-of-function of a patched gene, comprising:

- a. contacting one or more test agents with a cell that expresses a wild-type patched protein and identifying test agents that change the level of patched-dependent intracellular signal transduction relative to the absence of test agent;
- contacting test agents identified in step (a) with a cell having a patched loss-of-function phenotype and selecting those test agents that reverse at least in part the patched loss-of-function phenotype; and
- preparing a formulation including a test agent selected in step (b) and a pharmaceutically acceptable diluent.